An Introduction to 5-fluorouracil and its effects on *crithidia fasciculata*

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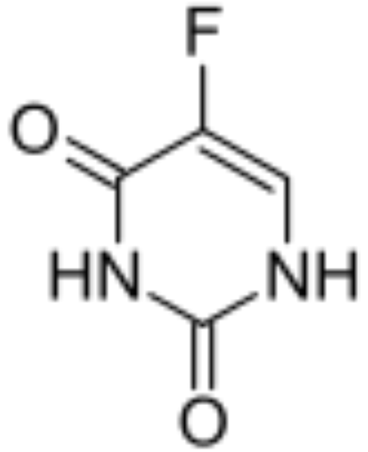
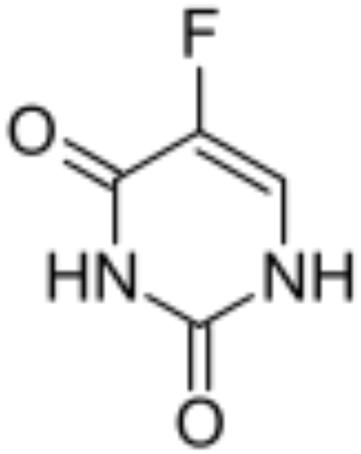
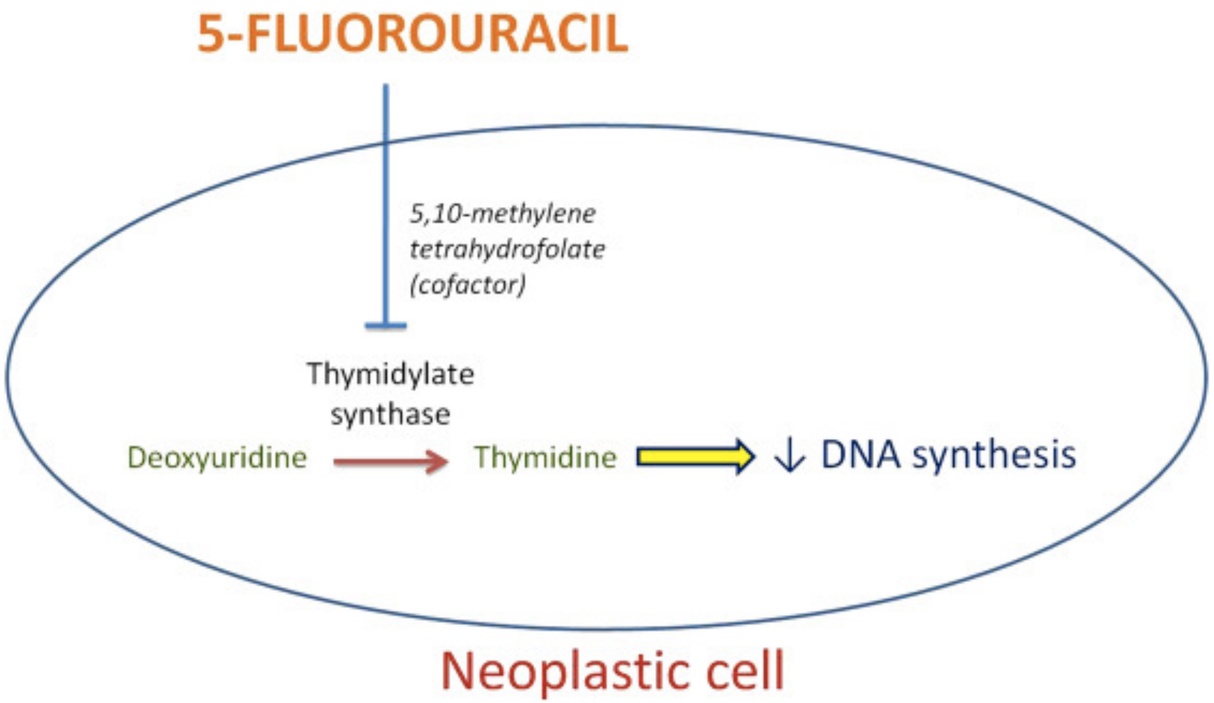
Fluorouracil

- medication used in chemotherapy
- works as a **thymidylate synthase (TS) inhibitor**, used to block synthesis of pyrimidine thymidine
- 5-FU causes a decrease in dTMP, which induces thymineless cell death



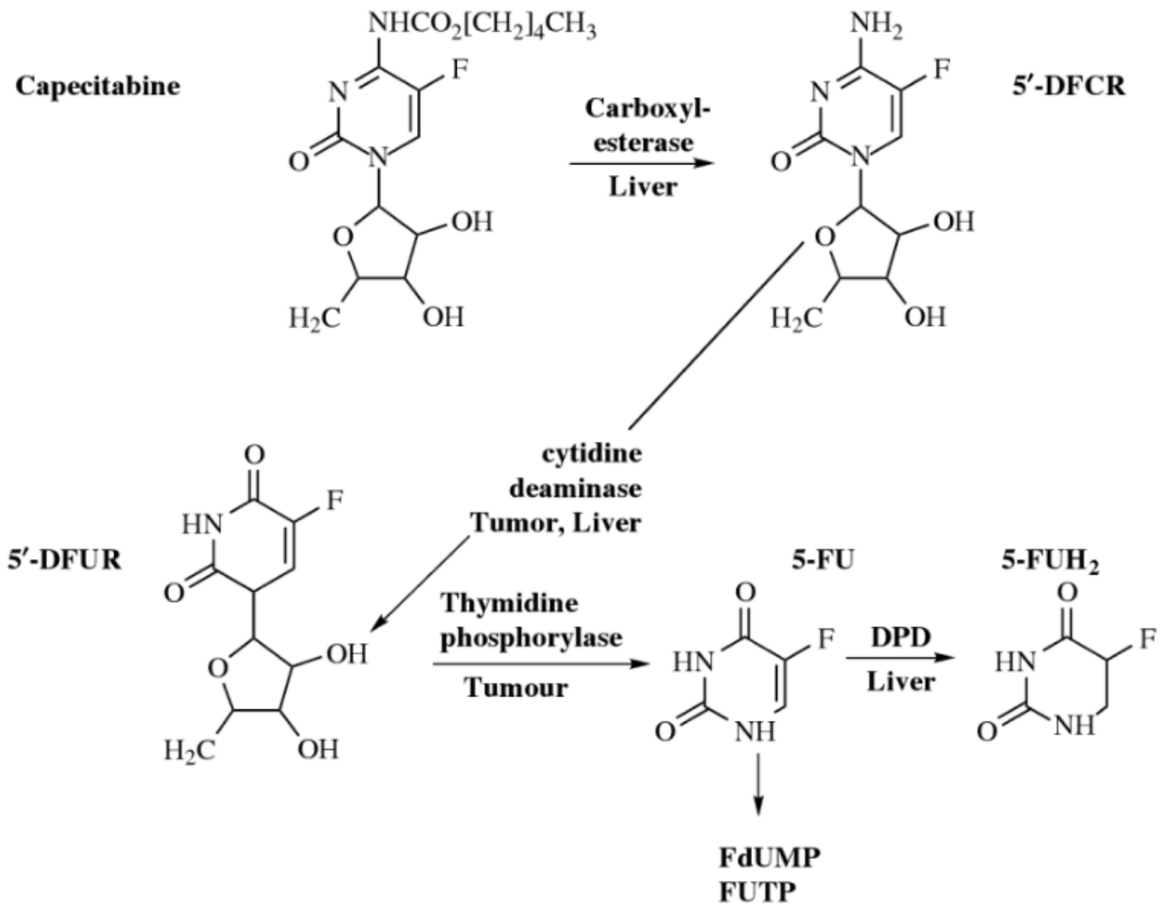
Fluorouracil





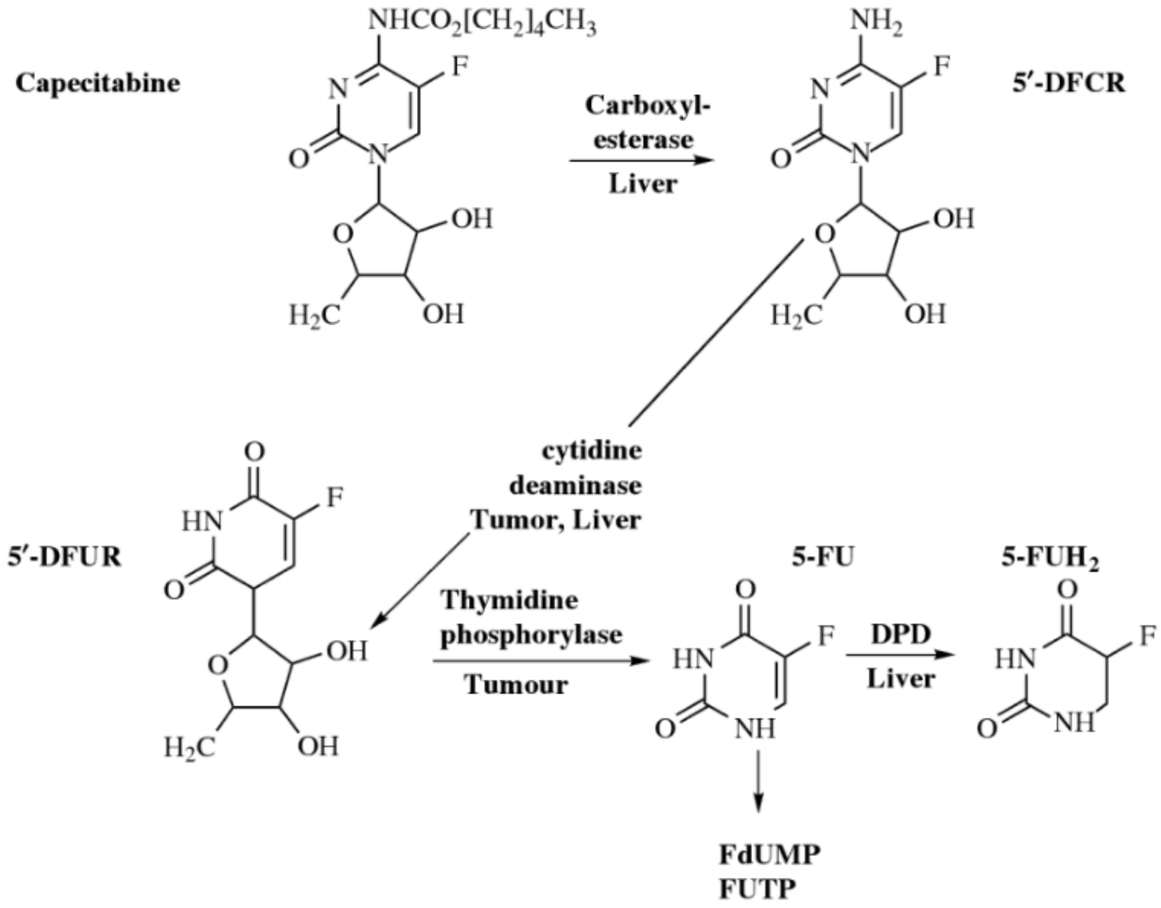
Activation of 5-fU

- Capecitabine: an orally administered prodrug of 5-FU
- Capecitabine is converted by carboxyl esterase (liver) to 5-DFCR and then to 5-DFUR by cytidine deaminase
- Cytidine deaminase expressed in both liver and tumor
- 5-DFUR converted to 5-FU by thymidine phosphorylase



Activation of 5-fU

- tumor specificity: because thymidine phosphorylase is expressed in a high level in malignant tumors relative to normal tissue



Fluorouracil ：common usage

Colon and rectal cancer

Anal cancer

Breast cancer

Gastrointestinal cancers including: anal, esophageal, pancreas and gastric cancer

Head and neck cancer

Unknown primary (squamous cell)

Neuroendocrine tumors

Thymic cancers

Cervical cancer

Bladder cancer

Hepatobiliary cancers

Adverse effects

Nausea
Vomiting
Diarrhea
Headache
Alopecia (hair loss)
Photosensitivity
Itch
Cardiotoxicity
Persistent hiccups
Mood disorders (irritability, anxiety, depression)

Crithidia fasciculata

- Trypanosome parasite
- Infects mosquitos
- Related to the parasites *Trypanosoma brucei gambiense* and *Trypanosoma cruzi,* which cause African Sleeping Sickness and Chagas' disease.

Fluorine NMR

- Utilizes nuclear magnetic resonance (NMR) to identify ^{19}F
- Real time FNMR used to measure the presence of the drug (5-fluoruracil) in the supernatant of the cells over time
- Height of the peaks indicate relative concentration

Fluorouracil on *Crithidia fasciculata*

- **Hypothesis**: Fluorouracil will affect the growth rate of parasite
- **Treatment**: *Crithidia fasciculata* + different fluorouracil concentration
- **Experiment**: *Crithidia fasciculata* were incubated in 5-FU in DMSO solution (5mmol, 1mmol, 0.2mmol, 0.04mmol, 0.008mmol or 0.0016mmol). Data were collected from OD600 growth curve
- **Result**: the growth rate of *Crithidia fasciculata* in 5-FU in DMSO solution with different concentration showed no significant difference
- **Conclusion**: 5-FU does not show an effect on *Crithidia fasciculata*

References

- https://lh3.googleusercontent.com/proxy/2NHX3-3ONp7PF3Z19NyUo-_VrED9n2i9St8GEhqzp50z0wkj09T7t7IdxQPMXwEnVE4_FSEPpTIHB2qxN2FjUy_rVQJ1w0U_2DBeHxEbsLGLk6ZjwyhcpQ
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